Emerald Health Pharmaceuticals' Cannabinoid-Derived Drug Shows Potential for Remyelination and Disease Modification for Multiple Sclerosis

Journal of Neuroinflammation paper highlights anti-inflammatory and neuroprotective properties of EHP-101 and potential to treat both relapsing-remitting as well as progressive MS

SAN DIEGO, CA, March 21, 2018 – Emerald Health Pharmaceuticals Inc. (EHP) announced today the published results of a study supporting the potential of its drug candidate, EHP-101 (previously known as VCE-004.8), to treat multiple sclerosis (MS). EHP-101 is a patented derivative of cannabidiol (CBD) modified to affect peroxisome-proliferator activator receptor gamma (PPARγ) and cannabinoid receptor 2 (CB_2) as well as the hypoxia inducible factor (HIF) pathway. These receptors and physiologic pathways are well documented in multiple peer-reviewed publications to be validated targets relating to inflammatory and neurodegenerative processes associated with MS and other neurodegenerative diseases. The study showed that EHP-101 reduced neuroinflammation, prevented demyelination and nerve cell damage, and may enhance remyelination, as suggested by complete recovery of motor activity in an animal model.

These results were published in *Journal of Neuroinflammation* in a paper entitled, "Hypoxia mimetic activity of VCE-004.8, a cannabidiol quinone derivative: implications for multiple sclerosis therapy." Co-authors of this paper included Eduardo Muñoz, MD, PhD, Chief Scientific Officer, Giovanni Appendino, PhD, Scientific Advisor, and Mari-Luz Bellido, PhD, Vice President of European Operations for EHP.

"There are no approved drugs capable of reversing MS and very limited treatment options for the more severe and progressive forms of MS. We have observed positive preclinical results with EHP-101, dramatically reversing the debilitating effects of MS in animals," said Jim DeMesa, MD, CEO of Emerald Health Pharmaceuticals. "Our scientists' pioneering work provides us the opportunity to advance unique treatment regimens for different stages and forms of MS."

Researchers evaluated the anti-inflammatory and neuroprotective properties of EHP-101 in two animal models of MS, one reflecting the most common early stage disease, the other representing a more aggressive form of the disease, primary progressive MS. In the model representing early stage disease the clinical manifestations of MS were attenuated in mice receiving EHP-101. In the model mimicking primary progressive MS, mice whose motor activity had declined to very low levels completely recovered to normal levels of motor activity. Assessing demyelination and nerve cell (axonal) damage, which are considered the histopathological hallmarks of MS, demyelination was significantly prevented in EHP-101-treated mice, while intense spinal cord demyelination was found in the untreated control group. Axonal disorganization was prevented by the treatment and the drug inhibited expression of proinflammatory markers.

"Our cannabinoid derivatives are designed to improve bioactivity and therapeutic utility of their natural precursors and it is clear that EHP-101 is achieving mechanistic outcomes that could be an important step for MS science," said Eduardo Muñoz, PhD, EHP's Chief Scientific Officer and Professor of Immunology at the University of Córdoba. "Our molecularly-modified CBD derivative modulated neuroinflammation and suggested an ability to enable remyelination based on the complete turnaround of motor activity observed in the animals in this study."

EHP is currently developing two drug candidates from its portfolio of cannabinoid analogs, one derived from CBD for multiple sclerosis and scleroderma, EHP-101, and one derived from cannabigerol (CBG), EHP-102, for Huntington's disease and Parkinson's disease. Additional data were previously published in two papers in the journal *Scientific Reports,* a *Nature* publication, as well as *Journal of Neuroinflammation*. EHP plans to start a human study in H2 2018 for multiple sclerosis and scleroderma, and expects to begin clinical-enabling studies for Parkinson's disease and Huntington's disease by 2019.

About Multiple Sclerosis and EHP-101

MS is one of the most common acquired neurological diseases in young adults. The National Multiple Sclerosis Society estimates there are 900,000 patients with MS in the seven major markets.

Disease progression is considered the result of two related processes, namely myelin destruction (demyelination) with failure to remyelinate and progressive axonal damage, with little capacity for recovery. Exacerbated innate and adaptive immune responses contribute to the pathophysiology of the disease and the majority of current therapies for MS are directed towards modulation of the immune response. Novel therapies to enable axonal remyelination are urgently needed. Hypoxia-inducible factor (HIF)-1α activation may exert anti-inflammatory capabilities and may be also linked to neuroprotection and remyelination[1].

While CBD has been shown to have anti-inflammatory, neuroprotective, and anti-oxidant effects that may act on neurodegenerative diseases such as MS, EHP-101 builds on the natural cannabinoid. It is an aminoquinone derivative of CBD endowed with dual peroxisome proliferator-activated receptor-γ (PPARγ) and cannabinoid receptor type 2 (CB2) activity, which are both validated therapeutic targets for MS. EHP-101 also targets the HIF pathway, expanding the rationale for its development as a novel MS drug.

About Emerald Health Pharmaceuticals Inc.

Emerald Health Pharmaceuticals is developing product candidates derived from cannabinoids for the treatment of CNS, autoimmune, and other diseases. The company has two families of new chemical entities, based on cannabidiol, CBD, and cannabigerol, CBG, that it has modified through rational drug design to affect validated receptors pertinent to targeted diseases. Its first drug candidate, EHP-101, is focused on treating multiple sclerosis and scleroderma. Its second, EHP-102, is focused on treating Huntington's disease and Parkinson's disease. The company is advancing preclinical development with the intent to launch a Phase 1 clinical study in 2018.

For more information, visit www.emeraldpharma.life or contact: info@emeraldpharma.life.

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[1] Yao SY, Soutto M, Sriram S. Preconditioning with cobalt chloride or desferrioxamine protects oligodendrocyte cell line (MO3.13) from tumor necrosis factor-alpha-mediated cell death. J Neurosci Res. 2008;86:2403–13.

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